Phosphatidylcholine in the treatment of localized fat

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Abstract

Phosphatidylcholine was initially used in emergencies and in the treatment of atheroma plaques in cardiac diseases. Recently, it has also been used in the treatment of localized fat deposits. We report on the authors' clinical experience of the use of 250 mg/ml phosphatidylcholine injections in the treatment of subcutaneous fat deposits, showing the clinical response and side-effects. Volunteers received phosphatidylcholine injections in several areas of localized fat deposits, with a minimum interval of one week and mean interval of 15 days between applications. Laboratory tests were performed during the period of the drug use. Clinical results reflect that phosphatidylcholine was efficacious in reducing the fatty pads in the treated areas, with few side effects. From the authors' point of view, the off-label use of phosphatidylcholine in the treatment of fatty pads and small areas of localized fat is safe, low cost, and effective.

Introduction

Phosphatidylcholine is a phospholipid extracted from soybean lecithin present in abundance in cell membranes, actively participating in the structure and transport between the cells (1).

This substance can alter cholesterol and other triglyceride metabolisms. It seems to be able to increase cholesterol solubility, alter the composition of fat deposits, and inhibit plaque aggregation (1). For these reasons, phosphatidylcholine is used in the intravenous treatment of lipid atheromas, hypercholesterolemia, fat embolism, fatty deposits or plaque adhering to arterial walls, mental disturbances, hepatic and cardiac conditions induced by medication, alcohol, pollution, virus, and toxins (2-10).

The cosmetic use of phosphatidylcholine originated in Italy. Its first use for such purposes was reported by an Italian physician named Sergio Maggiori, at the Fifth International Meeting of Mesotherapy in 1988, held in Paris, France. He presented his work with phosphatidylcholine in the treatment of xanthelasmas (11). In Brazil, the cosmetic use of phosphatidylcholine began at the end of the 1990s on an off-label basis.

Although the injectable form of phosphatidylcholine has not been approved for cosmetic purposes in Brazil, there is clinical evidence of its efficacy in treating localized fat. It has been widely used in Brazil in various clinical conditions where there are fat deposits in the subcutaneous tissue. These conditions are treated conventionally by liposuction or dermolipectomy. Phosphatidylcholine seems to be efficacious and effective in these cases, representing a new, less invasive, and potentially promising treatment for conditions which include "buffalo-hump" (an unaesthetic condition related with HIV fat redistribution syndrome, or FRS), lipomas, eye bulging (12), and xanthelasmas. Other possible therapeutic applications include localized fat on the thighs, hips, abdomen, flanks, neck, and lower third of the face.

Cautious about the use of phosphatidylcholine in the treatment of localized fat deposits, the Brazilian National Agency of Health Inspection (ANVISA), which regulates the use of medication in Brazil, published a resolution on January 9, 2003 prohibiting the use of this medication at the national level (13). Recently, this product has been used in Brazil not only by physicians, but also by laypersons, in non-medical locations such as gyms, beauty salons, etc.

The lack of research and publication on the subject and the apparent disinterest of the manufacturer (Aventis Pharma[R]) represent additional factors that have contributed to the non-regulation of cosmetic use of phosphatidylcholine in Brazil and, perhaps, the world. To date, there are no published articles or research studies reporting clinical, histopathological and laboratory data that prove the effectiveness of phosphatidylcholine in the treatment of localized fat areas. A study by Rittes shows photographs of pre and post phosphatidylcholine application in

fat pad cases (12) but does not report either the doses used or side effects. Another study, presented by one of the present authors (Serra) in a poster at the Workshop on Lipodystrophy in Athens in 2001 (14), showed this treatment on two HIV/AIDS patients with buffalo-hump and fatty pads, with good results. Temporary edema and erythema were the only side effects presented.

Action Mechanism

The action mechanisms of phosphatidylcholine injections in the subcutaneous tissue have not yet been explained. It is supposed that the medication penetrates the adipocyte through the double lipid layer, acting as an emulsifying/tensoactive agent (15). The physical-chemical characteristics of the stored lipids would therefore be altered, making them water soluble. This would permit their elimination due to their non-compatibility with the material stored in the adipocyte which is liposoluble. However, there are no histological and/or pharmacodynamic studies that ratify such a supposition.

Toxicity

The authors' experience in the cosmetic use of phosphatidylcholine has been short. However, the long-term safety of a drug may be assessed by drawing a comparative parallel to the safety of the drug itself, in this case phosphatidylcholine, when used for other, non-cosmetic ends. The doses used by the present authors do not exceed those considered safe for those therapeutic ends described above.

Highly purified phosphatidylcholine extracts from lecithins contained in egg yolk and soybean are used to prepare the oily parenteral nutrition emulsion (16). It has been described that in an infusion containing 1.2% phosphatidylcholine extract from egg yolk and 55% glucose (1 ml/kg/min) given to cats, there was a low incidence of side effects. Therefore, phosphatidylcholine was considered non-toxic for parenteral use (16).

The first reports of cardiological use of phosphatidylcholine (Lipostabi[R] by Aventis Pharma) are from the 70s. The drug was administered orally and parenterally, mainly by Italian and Russian physicians (17,18). The capacity of phosphatidylcholine to reduce blood cholesterol as well as high and low lipoprotein levels was reported (7,17). Klimov et al. compared the efficacy of Lipostabil[R] with that of nicotinic acid for the treatment of patients with hyperlipoproteinemia. They found that while both medicines reduced the intensity and incidence of angina pectoris, only phosphatidylcholine offered an effective treatment with minimum side effects (19).

Laboratorio Magistral, a Brazilian company which manufactured and distributed phosphatidylcholine among Brazilian physicians, claimed there was no acute or subchronic toxicity with doses up to 25 times the maximum. However, no studies were presented to corroborate this claim.

Commercial Presentations

Phosphatidylcholine is presented in two forms: the commercial product (Lipostabil[R] or Essentiale[R] (Natterman International GMBH), approved for cardiological use in some countries in Europe), and the manipulated medication, prepared under medical prescription. The latter should meet the quality and safety criteria established by competent authorities, regarding formulation described in Law 344, RDC 33 (when manufactured in Brazil) or competent bodies in other countries (15,20-22).

Materials and Methods

In the patient selection, the presence of certain physical conditions that could contribute to the occurrence of side effects was investigated. The exclusion criteria included the following: allergic antecedents to one of the components of the formula, pregnancy and lactation, active kidney or hepatic disease, mellitus diabetes or thyroid disease, obesity (assessed by the body mass index, BMI), moderate to severe loose skin or flaccidity, previous surgeries, and the presence of fibrosis or adherence in the areas to be treated.

From July 2001 to December 2002, the total number of treated patients was 213, of which 8 patients were HIV/AIDS positive.

Two hundred and five patients with different patterns of localized fat deposits on the body (thighs, hips, abdomen, flanks) and/or face (chin region) were submitted to treatment with phosphatidylcholine.

The patients were submitted to 1 to 5 treatment sessions with an average interval of 15 days between each session. The medication administered (250 mg/ml phosphatidylcholine, manufactured by the Laboratorio Magistral) was injected pure or diluted in saline solution (0.9%), depending on the extension of the area to be treated. The injections were made in the subcutaneous tissue using 30 G needles and 3 ml syringes. The depth of the application was 1 to 2 cm below the cutaneous surface and 0.2 ml was applied at each point with a distance of 2 cm between the points. The total volume of phosphatidylcholine injected varied according to the quantity of localized fat deposits in each patient, but in all cases no more than two vials (10 ml) were applied per session.

At each treatment session, digital photographs were taken of the patient's front view, back view, and profile, according to the area to be treated. In some patients the thickness of the fatty pad was measured with a specific ruler.

Buffalo-hump and other areas of localized fat

Eight HIV/AIDS patients with areas of fat accumulation due to FRS were submitted to treatment with phosphatidylcholine injections. Two of these patients presented only buffalo-humps; three presented buffalo-humps with fat deposits on the thorax, abdomen, and back; one with a buffalo-hump and fat accumulation in the chin and under-jaw region; one with a large lipoma on the back; and one with fat accumulation on the masseteric region.

The patients were submitted to 2 to 5 sessions with an interval of 30 days between each session. Phosphatidylcholine (250 mg/ml) was infiltrated at the subcutaneous level at a depth of 1 to 2 centimeters from the skin surface in the fat deposit areas. The area to be treated was marked out with equidistant points of approximately 1.5 cm, and 0.2 ml of the product was applied at each point. The total volume injected varied with the quantity of lesions to be treated per session, but did not exceed the recommended safety doses. Depending on the location and size of the lesions to be treated, anthropometric measurements and/or measuring by skin pinching and folding of the lesions were used to assess the results of the treatment.

Post-application care

Some recommendations were suggested to patients to reduce the symptoms caused by the injections and to speed fat absorption:

1) Compression of the treated area: the use of modeling belts or compressive clothing after application produces a draining effect, reducing edema.

2) The use of analgesics: acetaminophen was recommended for the first 24 to 48 hours.

3) Lymphatic drainage: can be used to help edema and fat absorption. It should be performed by an experienced professional under medical supervision, within two days following the injections.

In the case of the HIV/AIDS patients, the use of bandages, massage, and analgesics was not recommended. They were considered unnecessary, as the size and location of the lesions varied greatly and the lesions regressed slowly.

Laboratory tests

Thirteen of the 205 cosmetic (non HIV/AIDS) patients treated for localized fat deposits underwent laboratory tests during the treatment with phosphatidylcholine. The lipid, hepatic, renal profiles, and hemograms of these patients were assessed.

Graph I shows the result profiles at three different times during the treatment. The eight HIV/AIDS patients also underwent laboratory examination.

[GRAPHIC OMITTED]

Results

The mean results of the each test performed (pretreatment, 48 hours after, and 14 days later), relative to the cosmetic patients, are shown in graph 1.

The clinical response to the phosphatidylcholine injections was assessed on the thighs, hips, abdomen, flanks, chin region, and other areas of the face by photographic analysis and by measuring the weight, BMI, and fatty deposit thickness.

In the first 24 to 48 hours after application, the region presented moderate to severe edema, erythema, and localized heat. The reported discomfort was slight and abated with administration of common analgesics (acetaminophen or dipyrone in usual doses). Anti-inflammatory agents were prescribed for some patients for the first 48 hours. Some points showed bruises that regressed spontaneously in 7 to 10 days.

Slight to moderate itching at the application points was also reported by some patients.

Following the regression of the edema, softening was evident in all the treated areas. In the vast majority of patients, there was a reduction in subcutaneous thickness and the dimensions changed within up to 5 applications, at an average interval of 15 days. Few patients failed to notice reduction in the subcutaneous thickness.

In the case of the buffalo-humps of the HIV/AIDS patients, the lesions began to regress after the first session, and became less hard. All the patients with buffalo-humps reported significantly reduced discomfort and greatly improved neck movement. After the third session a considerable improvement in the lesion was noted, and after the fifth session an improvement of approximately 80% or the complete remission of some lesions was observed.

Discussion

Localized fat deposits, especially in women, are a cause of discomfort and anguish, leading patients to undergo surgical procedures such as liposuction and dermolipectomy to improve the cosmetic aspect. In countries with a tropical climate, such as Brazil, the anguish is compounded by the incentive to expose a perfect body. Fearful of extensive surgery and its complications, patients and physicians seek less invasive methods that may offer some results. Phosphatidylcholine has emerged as a safe and efficacious alternative method to achieve the reduction of small localized fat deposits on the face and body.

The adverse reactions observed after phosphatidylcholine injection in the adipose tissue were transitory, and no serious, systemic, or permanent complications were observed. The side effects usually appeared 2 to 5 days after applications, but the time varied depending on the metabolism of each individual. Several factors may determine lack of success or greater risk of side effects, such as incorrect antisepsis, use of medication of dubious origin, total doses above those considered safe, excessive injection volume at each point, inappropriately small distance between the points, superficial injections less than 1 cm below the epidermal surface, lack of pre- and post-application care, and perhaps most importantly, administration of the medication by unqualified persons. Among the possible complications that may also occur are infections, allergic reactions, tissue necrosis, and irregularities on the body surface (nodules and depressions).

The authors' clinical experience, reported in this article, followed the known use criteria for the drug, even though empirical for cosmetic purposes. No more than 2 vials were used (total of 10 ml) per session, in a total of 5 sessions of treatment, with an interval of more than 10 days between the applications. These measures were taken to avoid adverse systemic effects of the medication that may result from excessive doses or short intervals between injections.

All tests performed before and after treatments showed no significant alterations in either the hepatic function or the lipid profile. Wider studies are needed to ensure drug safety when injected subcutaneously. In the authors' experience, phosphatidylcholine has not been shown to be hepatotoxic and did not cause alterations in the lipid metabolism when used in the reduction of the subcutaneous thickness and in the used doses. Some patients may present alterations in the laboratory examinations, such as those suffering from diabetes, dyslipidosis, morbid obesity, and endocrine diseases, and those who already have some degree of hepatic overload. For these patients, caution and extensive laboratory control are necessary in choosing to treat with phosphatidylcholine injections.

The alterations in the lipids found in some HIV/AIDS patients, such as increases or decreases in total triglycerides and both HDL and LDL cholesterol, may not be related to the treatment with phosphatidylcholine but rather to dyslipidosis, common to the FRS caused by some anti-retrovirals; for the same reason the CD4 and CD8 cell counting were compatible with the moment of treatment in the HIVAIDS patients.

The greatest obstacle to phosphatidylcholine use is the limited knowledge of its pharmacology in the subcutaneous tissue. Another is the potential for overuse, which may alter the medical status of the substance, encouraging widespread skepticism in the medical community and leading to the prohibition of its use, making research and clinical experiment impossible.

While not drawing a direct comparison, the authors would like to point out that similar cases have occurred with other drugs, such as botulinum toxin, which has been used for cosmetic purposes since 1990. However, the permitted off-label use allowed physicians to study the drug and its benefits in wrinkle treatment for over 10 years before the FDA finally approved its cosmetic use in 2002.

Conclusions

Phosphatidylcholine was shown to be efficacious and safe in the indications described, and can substitute for liposuction in some specific indications. Its use by medical and experienced professionals is crucial for safety and good results.

As with any other medication, it needs wide investigation protocols for new indications and long-term studies, so that the recommended dose and safe application technique can be standardized.

Liposuction and excision surgery have been the standard alternatives for treating humps and lipomas in HIV/AIDS patients. It should be considered that these lesions recur frequently and consequent ly the procedures need to be repeated. Thus, phosphatidylcholine injections may represent a safer alternative treatment for lesions caused by fat accumulation in these individuals. It is a low cost, efficacious, and easy application method as compared to surgical alternatives.

References

(1.) Strayer L. Estrutura e Dinamica das Membranas. Bioquimica, Third Edition. Guanabara Koogan, Rio de Janeiro,1996; 246-247.

(2.) Navder KP, Baraona E, Lieber SC. Polyenylphosphatidylcholine decreases alcoholic hyperlipemia without affecting the alcoholinduced rise of HDL-cholesterol. Life Sci 1997; 61(19):1907-14.

(3.) Maranhao RC, Feres MC, Martins MT, Mesquita CH, et al. Plasma kinetics of a chylomicron-like emulsion in patients with coronary artery disease. Atherosclerosis 1996; 27:126(1): 15-25.

(4.) Bialecka M. The effect of bioflavonoids and lecithin on the course of experimental atheroselerosis in rabbits. Ann Acad Med Stetin 1997; 43:41-56.

(5.) Brook JG. Linn S, Aviram M. Dietary soya lecithin decreases plasma triglyceride levels and inhibits collagen and ADPinduced platelet aggregation. Biochem Med Metab Biol 1986; 35(1):31-9.

(6.) Melchinskaya EN, Gromnatsky NI, Kirichenko LL. Hypolipidemic effects of Alisat and Lipostabil in patients with diabetes mellitus. TERAPEVTICHESKII ARKHIV 2000; 72 (8):57-58.

(7.) Ozerova IN, Paramonova IV, Akhmedzhanov NM. Perova NV. Sinvastatin and Lipostabil induce beneficial changes in high density lipoproteins phospholipid composition. Atherosclerosis 1999; 144(supl 1):33.

(8.) Polichetti E, Janisson A, La Porte PL, Portugal H, et al. Dietary polyenylphosphatidylcholine decreases cholesterolemia in hypercholesterolemic rabbits--role of the hepato-billiary axis. Life Sciences 2000; 67(21):2563-2576.

(9.) Takahashi Y, Mizunuma T, Kishino YJ. Effects of choline deficiency and phosphatidylcholine on fat absorption in rats. Nutr Sci Vitaminol 1982; 28(2): 139-47.

(10.) Simonsson P, Nilsson A, Akesson B. Postprandial effects of dietary phosphatidyleholine on plasma lipoproteins in man. Am J Clin Nutr 1982 Jan; 35(1):36-41.

(11.) Maggiori S. Traitement mesoterapique des xanthelasmas a la phosphatidilcoline poluinsaturee (EPL). V Congres Internacional de Mesotherapie, Paris: Dermatologie, 1988; 364.

(12.) Guedes P. The use of phosphatidylcholine for correction of lower lid bulging due to prominent fat pads. Dermatol Surg 2001; 27(4):391-392.

(13.) Resolution n[degree] 30, of January 08, 2003. DOU 09.01.2003.

(14.) Serra M. Pereira FB. Subcutaneous infiltration with phosphatidylcholine solution for treatment of "buffalo hump" and "fatty pads." 3rd International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV. Athens, Oct 2001, abstract P115.

(15.) Budavari S. Maryadele JO, Smith A, et al. The Merck Index. 12th ed. Merck Research Laboratories Division of Merck N Co. Inc. Whitehouse Station. NJ, 1996.

(16.) Lecithin. Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives. Wild Hlth Org. techn. Rep. Ser., 1974, No. 539; FAO Nutrition Meetings Report Series, No. 53, 1974.

(17.) Galeone FS, Salvadorini F. Pagliai E. et al. Effects of Soybean polyunsaturated phosphatidylcholine (Lipostabil) on Hyperlipoproteinemia. Curr Ther Research. 1978; 24(3):299-305.

(18.) Almazov VA, Freidlin lS, Krasil'nikova EI. Use of Lipostabil to correct lipid metabolism disorders in patients with ischemic heart disease. Kardiologiia 1986; 26(2):39-42.

(19.) Klimov AN, Konstantinov VO, Lipovetsky BM et al. Essential phospholipids versus nicotinic acid in the treatment of patients with type lIB hyperlipoproteinemia and ischemic heart disease. Cardiovasc Drugs Ther 1995; 9(6):779-84.

(20.) Administrative Order n[degrees] 344, of May 12, 1998. DOU 01.02.99.

(21.) Resolution n[degrees] 33, of April 19, 2000. DOU 24.04.00.

(22.) Todd RG, ed. 1962 Extra Pharmacopoeia-Martindale. 25th ed. London: The Pharmaceutical Press, 1998.